REMARKS

This application has been reviewed in light of the Office Action dated March 22, 2005. Claims 256-272 are now pending. Claims 256 and 264has been amended. Additionally, claim 272 has been added to provide Applicants with a more complete scope of protection. Support for amended claim 256 can be found, inter alia on page 511, line 20 through to page 512, line 3; and on page 518, lines 9-11. Support for new claim 272 can be found on page 332, lines 8-12. Additionally, the specification has been amended to recite the current status of the nonprovisional patent application to which this application claims priority. No new matter has been added by these amendments. Accordingly, applicants respectfully request that this amendment be entered.

Priority

The Examiner states that the present application lacks the necessary reference to the prior application and that the current status of all nonprovisional parent applications referenced should be included.

Applicants previously had included the necessary reference to U.S. Serial No. 10/066, 175, which claims the benefit of priority to U. S. Provisional Application No. 60/265,586, in a preliminary amendment filed on November 26, 2003. Additionally, Applicants, have amended the specification in this response to include the current status of the nonprovisional parent application, which is now abandoned. Applicants respectfully request that the November 26, 2003 amendment be entered, as well as the corrected status of U.S. Patent Application No. 10/066,175.

Information Disclosure Statement

Applicants acknowledge consideration of the information disclosure statement filed on November 26, 2003.

Claim 256-271 Are Rejected Under 35 U.S.C. § 112, Second Paragraph.

Claims 256-271

The Examiner states that claims 256-271 are rejected under 35 U.S.C., §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner alleges that Claim 256 is indefinite for reciting component "A" as including oxazolyl, thiazolyl, triazolyl, and triazinyl. The Examiner states that such terms are not exact and definite structures because each term has isomers, and therefore, their exact point of attachment to the main core has been excluded from the claim recitation.

Applicants respectfully disagree. Those skilled in the art will recognize appropriate points of attachment for these substitutents without being told specifically where those attachments are located. Because the scope of the claim is evident to an ordinary artisan, claim 256 is not indefinite under 35 U.S.C. §112, second paragraph.

Claim 268

The Examiner has objected to claim 268 alleging that "if claim 267 is allowed, claim 268 will be duplicate composition claim." (Page 2, paragraph 6).

Applicants disagree that the claims are duplicative. Claim 267 is drawn to a pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 256 and a pharmaceutically acceptable carrier. Alternatively, claim 268 is drawn to a

pharmaceutical composition made by combining a therapeutically effective amount of the compound of claim 256 and a pharmaceutically acceptable carrier. Because claim 267 is drawn to a composition claim and claim 268 is drawn to a product-by-process claim, claims 267 and 268 are not duplicative. Applicants respectfully request that the Examiner withdraw this rejection.

Claim 269

The Examiner states that claim 269 is related to the process of making a pharmaceutical composition, but remains silent by not reciting the exact process or steps required for making the composition. (Page 2, paragraph 7).

Applicants respectfully disagree. Claim 269 recites a process for making a pharmaceutical composition comprising combining a therapeutically effective amount of the compound of claim 256 and a pharmaceutically acceptable carrier. Because the term "combining" is recited, the process required for making the composition is included in the claim. Therefore, claim 269 is not silent as to its process, and Applicants respectfully request that this rejection be withdrawn.

Claim 264

The Examiner has rejected claim 264 because it "cannot be accommodated by the Formula of main claim 256 for the definitions recited for B component. Claim 256 remains silent about the hydrogenated form of phenyl i.e. cyclohexyl group." (Page 3, paragraph 8).

Applicants have amended claim 256 to recite "wherein B is phenyl and the phenyl is optionally substituted with one or more of the following: -F, -Cl, -Br, $-CF_3$, straight chained or branched C_1-C_7 alkyl, **C_3-C_7 cycloalkyl.**" Claim 264, as amended, appropriately depends on claim 256, thereby rendering this rejection moot.

Claims 270-271

The Examiner has rejected claims 270-271 because these claims recite a "method of treating a subject suffering from a disease(s), which are not exactly and definitely defined." Additionally, the Examiner states that the claims "remain silent about the exact amount of the compound of claim 256, and also about the definite and exact process of administration. Claims also do not state anything about the pharmacological properties inherent to compounds." (Page 3, paragraph 9)

Applicants respectfully disagree. First of all, the diseases of anxiety and depression are defined in the specification. As stated on page 2, lines 6-10, depression is "a markedly gloomy mood in which there is a loss of interest in life, and general feelings of hopelessness and worthlessness. Depressive symptoms range in severity from mild mood swings to severe delusions about self-worth, accomplishments, and the future." Additionally, anxiety is also defined on page 3, lines 1-7 as "relat[ing to] psychological and physical manifestations...not attributable to real danger and occurring either in attacks (panic disorder - PD) or as a persisting state (generalized anxiety disorder -GAD)." Secondly, the claims do describe the amount of the compound to be administered as the "amount of the compound of claim 256 effective to treat" subject's depression or anxiety. An 'effective amount' of the compound is defined on page 124, lines 24-27 through to page 125, lines 1-2. The term "effective amount" has been held not to be indefinite. For example, In *Ex parte Skuballa*, 12 USPQ2d 1570 (Bd. Pat. App. & Inter. 1989), the Board held that a pharmaceutical composition claim which recited an "effective amount of a compound of claim 1" without stating the function to be achieved was definite, particularly when read in light of the supporting disclosure which provided guidelines as to the

intended utilities and how the uses could be effected. In the instant specification, not only is the term defined, but the function is provided.

Additionally, modes of administration are described, inter alia, in the specification on page 128. For example compounds can be administered by intramuscular, intrathecal, epidural, intraperitonial or subcutaneous injection (lines 9-11) and orally (line19). Therefore, the process of administration is defined.

Finally, pharmaceutical properties, such as therapeutic properties, are described in the specification, as well. For example, on page 125, at lines 3-15, the uses of the instant compounds for treating depression and anxiety are discussed.

Because the specification defines the diseases in claims 270 and 271, the amount of compound to be used, the process of administration and pharmaceutical properties, the claims are not indefinite. For these reasons, Applicants respectfully request that the §112, second paragraph rejection be withdrawn for claims 270-271.

Missing page in specification

The Examiner has stated that page 608 is missing in the specification. Applicant is including the missing page with this reply.

Claim 270-271 Are Rejected Under 35 U.S.C. § 112, First Paragraph

It is alleged that the specification, while being enabled for a single, definite and exactly defined disease, does not reasonably provide enablement for a generic subject's disorder(s) related to depression and anxiety, in part, because the claims are drawn to disorders that are not related and whose treatment mechanism is relatively unknown. (Page 3, paragraph 12, page 4, paragraph 14). Thus, the Examiner alleges that the specification does not enable any person

skilled in the art...to practice the invention commensurate in scope with these claims. (Page 3, paragraph 12). The Examiner also alleges, that for the many reasons provided, including the lack of a dosage regime, one of ordinary skill in the art could not practice the invention without undue experimentation. (Page 4, paragraph 14, page 6, paragraph 16).

Applicants strongly disagree. Applicants assert in the specification that the instant compounds, GAL3 receptor antagonists, are useful in the treatment of both depression and/or anxiety. In order to establish a prima facie case of nonenablement, the Office must explain why the specification is not enabled based on sound scientific reasoning or acceptable evidence which is inconsistent with the asserted statement. (*In re Marzocchi, 169 USPQ 367 (CCPA 1971)*

Applicants respectfully request the Office to provide evidence or scientific reasoning as to why a single claim drawn to anxiety or depression is enabled, but two claims, one drawn to anxiety and one drawn to depression are not enabled. Other than broad generalizations on pages 3-6 of the Office Action, no reasons have been provided by the Examiner as to why one of ordinary skill in the art would doubt the detailed teachings of the subject specification regarding the use of the instant compounds for treating anxiety and/or depression. Without such evidence, this determination is apparently arbitrary and without the substantiation as required by law. *Id.*

Moreover, nothing more than objective enablement is required. Objective enablement can be provided through broad terminology or illustrative examples. *In re Marzocchi, id at 369.*

Applicants contend that the instant specification does enable the present invention. For example, Applicants have provided numerous examples of instant compounds with selective GAL3 receptor binding. (Page 597-611). Additionally, in vivo animal models, the rat Forced Swim Test and the rat Social Interaction Test, which are predictive of efficacy in humans against depression and anxiety, respectively, have shown efficacy of the instant compounds. (541-596).

Moreover, in the "Experimental Details" section starting on page 355, over 200 examples are provided that discuss how to make the instant compounds. Furthermore, the specification teaches methods known to those of ordinary skill in the art for administration, dosage level, dosage form and formulation of the instant compounds and also provides guidance by teaching preferred methods. Specifically, with respect to formulations, on page 347, it is taught that pharmaceutical compositions comprising compounds of the invention contain at least about 0.01 mg to 800 mg, but more preferably between 1 to about 20 mg, of a compound of the invention. Pages 350 to 353 provide guidance on particular pharmaceutical carriers and adjuvants used in formulations. It is also taught that optimal dosages to be administered will vary and may be determined by those skilled in the art depending on factors which are listed thereafter. (page 353, lines 27-28).

Although the Examiner has cited references, allegedly to show the state of the art related to depression and anxiety, page 5, he has failed to provide references relating to the use of GAL3 antagonists in conjunction with anxiety and/or depression. The section entitled "Background of the Invention" in the instant specification, however, discusses numerous references linking anxiety and depression to the GAL3 receptor. (See the section in the Background entitled "Discovery of GAL3 receptor and its role in depression and anxiety" for references). Such references, in turn, led to a series of experiments resulting in the evaluation of selective GAL3 receptor antagonists to treat depression and anxiety. Alternatively, the Examiner has not provided state of the art references that would cause a skilled artisan to doubt that both anxiety and depression can be treated with GAL3 antagonists.

Applicants contend, therefore, that by using the teaching and guidance in the specification, including the instant compounds in conjunction with the art recognized rat Forced

Swim Test, the rat Social Interaction Test and the GAL3 affinity binding assay, together with additional known methods in the art, such those described herein-above, one of ordinary skill can practice the claimed invention without undue experimentation.

In view of the foregoing, the claimed invention is believed to be in compliance with 35 U.S.C. 112, first paragraph. Withdrawal of the rejection of the present claims is therefore proper and respectfully requested.

Conclusion

In view of the foregoing, Claims 256-272 are submitted to be allowable, and issuance of a formal Notice of Allowance is respectfully solicited.

Respectfully submitted,

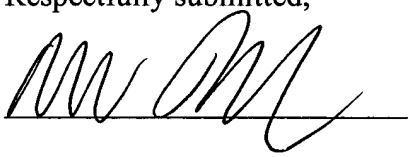

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Table 8: Antagonist selectivity ratios determined for the human GAL3 receptor vs. serotonin receptors and several transporters.

Example	hGAL3	$h5HT_{1A}$	$h5HT_{1B}$	$h5HT_{1D}$	$h5HT_{1E}$	$h5HT_{1F}$	$h5HT_{2A}$	$r5HT_{2C}$	$h5HT_{4}$	$h5HT_{6}$	$h5HT_{7}$	r5HT Uptk	rNE Uptk	rDA Uptk
11	1	>30	1	1	>100	20	>30	9	14	9	11	18	>100	>30
15	1	>30	7	17	>100	>30	>100	8	>30	20	>30	24	>100	>100
17	1	>30	5	12	>100	>100	>30	6	30	8	21	8	>100	>100
22	1	>100	>30	>30	>100	>100	>100	>30	>30	>30	>30	>100	>100	>100
34	1	>100	>30	>100	>100	>100	>100	>30	>100	>100	>100	>100	>100	>100
49	1	>100	>30	>30	>100	>30	>100	>30	>30	0	>30	>100	>100	10
60	1	>100	>30	>100	14	25	>100	21	14	>100	>30	>100	>100	>100
77	1	>30	5	9	>30	>30	28	6	17	6	20	10	>100	>30
92	1	>100	>100	>100	>100	>100	>100	ND	2	>100	ND	>100	>100	>100
94	1	>100	>30	>100	>100	>100	>100	>30	>30	>30	>100	>100	>30	>130
95	1	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100	>100
97	1	>100	>30	>100	>100	>30	>100	>30	>30	>100	>100	>100	>30	>100
98	1	>100	>30	>100	>100	>30	>100	>30	>30	>100	>100	>100	>100	>100

ND = Not determined